



ORIGINAL RESEARCH PAPER

Obstetrics & Gynaecology

EFFECT OF AMINO ACIDS INFUSION IN PREGNANT WOMEN WITH OLIGOHYDRAMNIOS

KEY WORDS: Amniotic fluid index (AFI), Oligohydramnios, Amino acids infusion

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ABSTRACT

Background: Adequate amniotic fluid is essential for normal fetal growth and fetal well being. Reduced amniotic fluid index (AFI), also called oligohydramnios, is associated with higher incidence of meconium staining, cesarean section due to fetal distress, abnormal fetal heart rate tracing, and result in lesser APGAR score, etc. Maternal nutrition had a definite role in molecular mechanism that's directly effects on fetus. Thus, under nutrition of various nutrients as amino acids, carbohydrates, essential fatty acids play a great role in the development of oligohydramnios and intrauterine growth restriction. Globally various trails have been done to explore the possibility of increasing the liquor amount and fetal weight by giving intravenous fluids of variety in the form of dextrose, maltose, amino acids etc. Improved maternal nutritional status by intravenous amino acid infusion appears to improve the AFI.

Materials and method: It is a prospective longitudinal study, 65 pregnant women of any gravida and parity of different age, with identified reduced amniotic fluid index (oligohydramnios) by ultrasonography were subjected to amino acids intravenous infusion daily along with 10% dextrose infusion for 7 days and ultrasound was repeated after 1 week. If required, they were called back for second round of infusion. Ultrasound was repeated to see whether it has any effect on AFI or not.

Results: 61.5% improvement in AFI was found in first round of infusion and 69.2% improvement in after second round of infusion. This finding was found to be statistically significant (p<0.05).

Conclusion: Improvement in maternal nutritional status by intravenous amino acid infusion appears to improve the AFI. Further study with a bigger sample size, drawing various confounding factors and with robust studies like RCT will be needed.

Background

Adequate amniotic fluid is essential for normal fetal growth and fetal well being. Normally amniotic fluid start producing right from the 12th days of conception and increase steadily and reaches peak volume at around 33 to 34 weeks¹. Reduced amniotic fluid, also called oligohydramnios, is associated with higher incidence of meconium staining, cesarean section due to fetal distress, abnormal fetal heart rate tracing, lesser APGAR score, etc. The various conditions associated with oligohydramnios are chromosomal abnormalities, uteroplacental insufficiency, congenital anomalies, pregnancy induced hypertension (P.I.H), intrauterine growth restriction (I.U.G.R), diabetes mellitus and post term pregnancy. Fetal abnormalities particularly involving the urinary tract are an important cause of early onset oligohydramnios².

About 8% of pregnant women can have low levels of amniotic fluid, with about 4% being diagnosed with oligohydramnios. It can occur at any time during pregnancy, but it is most common during the last trimester. If a woman is passed her date by two weeks or more, she may be at risk for low amniotic fluid levels since fluids can decrease by half once she reaches 42 weeks gestation. Oligohydramnios can complicate 12% of pregnancies that go past 41 weeks.

In 1987 a semi quantitative sonographic assessment of amniotic fluid volume (AFV) was developed known as Amniotic fluid index (AFI)³. This involves the summing of maximum vertical pockets in each of the four quadrants of the uterus.^{3,4}

Table 1: Diagnostic criteria for oligohydramnios⁵

Variables	AFI
Severe oligohydramnios	≤5cm
Borderline oligohydramnios	5.1 – 8 cm
Normal	8.1 – 24 cm
Polyhydramnios	>24 cm

Alterations in fetal nutrition and endocrine status may result in developmental adaptations that permanently change the structure, physiology, metabolism, and postnatal growth of the offspring.⁶ There is a growing evidence that maternal nutrition status can alter the epigenetic state (stable alternations of gene expression through DNA methylation and histone modification) of the fetal genome.⁷ Impaired placental synthesis of nitric oxide (a major vasodilator and angiogenic factor) and polyamines (key regulators of DNA and protein synthesis) may provide a unified explanation for the etiology of IUGR in response to maternal under nutrition and over nutrition.⁸ However, improvement in maternal nutrition may not have been achieved with diet alone because of non-compliance and socioeconomic status.⁹ Maternal nutrition have a definite role in molecular mechanism that's directly effects on fetus. Thus, under nutrition of various nutrients as amino acids, carbohydrates, essential fatty acids play a great role in the development of IUGR.¹⁰ Globally various trails have been done to explore the possibility of increasing the liquor amount and fetal weight by giving intravenous fluids of variety in the form of dextrose, maltose, amino acids etc. Improved maternal nutritional status by intravenous amino acid infusion appears to improve the AFI.¹¹

Methodology: A study was carried out in department of Obstetrics and Gynaecology, Jawaharlal Nehru Institute of Medical Sciences (JNIMS), Imphal, Manipur, between October 2017 to May 2019, to determine the outcome of amino acids infusion in pregnant woman with reduced AFI (<8cm diagnosed ultrasonographically) during 28 to 36 weeks of gestation period with intact membrane and not in labour. We excluded pregnant women with pregnancy induced hypertension, multiple pregnancy, pre-labour rupture of membrane, congenital anomaly, intrauterine fetal demise and patient having any chronic diseases like essential

hypertension, diabetes, major cardio respiratory diseases

After proper history taking, general and obstetrical examination, a provisional diagnosis of oligohydramnios had been made and such cases were sent for detailed ultrasonographic examination. Amniotic fluid volume was measured with 4 technique which consisting of measuring the largest pool of fluid found in each of the 4 quadrant of uterus. The added measures gave AFI. The fluid was said to be decrease if it was less than 8 cm and severely decreased if it was less than 5 cm. It was based on single scan if needed serial scan.

STUDY TOOLS or PROCEDURE

Pregnant woman with reduced AFI (isolated oligo hydramnios) was admitted in the ward and infused amino acids intravenously along with 10 % dextrose once daily for 7 days along with her daily administration of iron & folic acid, calcium, vitamins and normal recommended diets.

Thereafter, USG was done after one week from the last dose of infusion. Any USG finding was recorded. If needed (AFI < 8 cm), patients were called to the ward for another round of similar infusion and repeat USG scan for AFI and record the same as before. Any increase or decrease in AFI following amino acids infusion was noted.

SAMPLE SIZE:

Taking an incidence of 0.67%⁶¹ sample size was calculated as, Sample size = $1.96^2 pq / e^2$

Table 2: Distribution of the respondents by AFI before and after amino acids infusion

AFI	No. of patient before infusion	%	No. of pts.in 1 st USG after 1 st infusion	%	No. of pts.in 2 nd USG after 2 nd infusion	%
≤5cm	10	15.4	6+5=11	16.9	4+4=8	12.3
5.1-8cm	55	84.6	14 +4==18	27.6	11+3+2+1=17	26.1
>8cm	-	-	36	55.5	36+3+1=40	61.7
Total	65	100.0	65	100.0	65	100.0

Pts.:patients, USG:Ultrasound

From the table 2, patients with severe oligohydramnios (AFI≤5cm), out of 10 patients who were having severe oligohydramnios, 4 patients were found improved of AFI (>5.1cm) after 1st infusion but there was no improvement for 6 patients. But on subsequent 2nd infusions out of these 6 patients 2 patients increased in their AFI but 4 patients still remain below 5 cm. So, 4 patients of severe oligohydramnios remain unchanged after 2nd infusion which came around 40% (no improvement out of 10). A total of 5 patients with severe oligohydramnios got improved to moderate which contributed around 50%.

Out of 4 patients who improved to moderate from 1st infusion, one got improved to normal AFI after the second infusion. So only one patient got improved from severe to normal after 2nd infusion (1 out of 10) accounting to 10%.

From this table, regarding patients with moderate oligohydramnios, it also explained that, out of 55 patients who had moderate oligohydramnios (AFI 5.1-8 cm), 36 patients (65.4%) had improved AFI above 8 cm, but 14 remain more or less at same level and 5 patients rather reduced AFI to ≤5cm. After subsequent infusion it was found that 3 patients from those 14 patients who did not improve in first infusion got improved but 11 remain more or less at same level. So, a total of 39 patients (70%) with moderate AFI improve to normal after 2nd infusion. And out of 5 patient who reduced AFI to severe from moderate oligohydramnios despite amino acids infusion, 1 patient got improve in AFI after 2nd infusions and 4 remain below 5 cm. So, a total of 12 out of 55 moderate oligohydramnios remained same after 2nd infusion which came around 21.8%.

From above table, over all studies, it shows that 24.6% (16 out of 65) does not have significantly improved in their AFI

Where p=prevalence /incidence=0.67

q=100-p=99.33

e=absolute error=2

Sample size comes to 65

STATISTICAL ANALYSIS:

The data collected were checked for completeness then it was entered in Microsoft excel 2007. The data was analyzed using IBM SPSS version 16. Data were described using percentages. Test of significance was performed using chi-square test and Yate's correction was used when expected cell value was <20%. Cochran's Q test was used for comparing improvements after 1st and 2nd infusion to pre infusion. Probability value of less than 5 was taken as significant.

RESULT

Table 1: Distribution of the respondents by AFI

AFI in cm	Frequency	Percentage
≤5 cm (severe)	10	15.4
5.1-8 cm (moderate)	55	84.6
Total	65	100.0

Patients were divided as severe oligohydramnios (AFI ≤5cm) and moderate oligohydramnios (AFI 5.1- 8 cm). There were 10 patients with severe oligohydramnios and 55 patients with moderate oligohydramnios in the present study as given in table 1.

despites infusion given for 2 cycles and rather 6.1% (4 out of 65) reduced AFI despites 2 cycles infusion.

Table 3: Distribution of the respondents by AFI improvement after 1st and 2nd infusion

Intervention	Improved (%)	Not improved (%)	Total (%)	Cochran's Q test
Before infusion	0 (0.0)	65 (100.0)	65 (100.0)	Value =81.11 df-2 p-0.000
After first infusion	40 (61.5)	25 (38.5)	65 (100.0)	
After second infusion	45 (69.2)	20 (30.7)	65 (100.0)	

From the table 3 above, it is seen that after the first infusion there was 61.5% improvement and after the second infusion it improved to 69.2%. This finding was found to be statistically significant (p<0.05).

DISCUSSION

Women who are at risk for potentially adverse perinatal outcome can be identified by the assessment of amniotic fluid volume in antenatal period and amino acids infusion can be given. This prospective study was conducted among 65 pregnant women with oligohydramnios to determine the outcome of amino acids infusion in pregnant woman with reduced AFI/oligohydramnios.

In this study severe oligohydramnios was found in 15.38% of cases and so 84.6% of them had moderate oligohydramnios. This finding was in concordance with the study by Gupta R et al¹² where severe and moderate oligohydramnios was found in 16% and 84% respectively. In the study by Shree P et al¹³, 33 (66%) patients had borderline oligohydramnios (AFI 5 – 8 cm)

while 17 (34%) patients had severe oligohydramnios (A.F.I <5 cm). Same finding was also noted in the study by Baxi M et al¹⁴. After the final infusion, 45 patients were improved from their baseline AFI which contributed 69.2% in this study. In the study by Meetanpreet et al¹⁵, similar finding was noted i.e. 70% cases of reduced AFI cases improved so majority of the cases improved in AFI in both the studies.

There were 4 cases of severe Oligohydramnios and 21 cases of moderate Oligohydramnios at the time of their first visit in the study by Gupta R et al¹². After amino acid infusion therapy, on repeat ultrasonography, 9 (36%) cases patients with moderate Oligohydramnios had improved amniotic fluid index (AFI) to normal whereas two patients (50%) with severe Oligohydramnios had improved A.F.I. to moderate Oligohydramnios and remaining 12 and 2 patients of moderate and severe Oligohydramnios group patients did not show any changes in A.F.I. In this study, out of 55 patients who had moderate oligohydramnios (AFI 5.1-8 cm), 36 patients (65.4%) had improved AFI above 8 cm, but 14 remain more or less at same level and 5 patients rather reduced AFI ≤5cm. After subsequent infusion it was found that 3 patients from those 14 patients who did not improve in first infusion got improved but 11 remain more or less at same level. So, 39 patients (70.9%) improved to normal from moderate oligohydramnios in this study which was higher from Gupta R et al¹² study. But similar finding was observed in this study regarding severe oligohydramnios that 5 patients with severe oligohydramnios got improved to moderate which contributed around 50%. There was improvement in 69% of the cases with oligohydramnios after the second infusion in this study.

In the study by Ahmad A, out of 5 patients with severe oligohydramnios 2 patients (40%) improved to moderate level and out of 15 patients with moderate oligohydramnios 5 patients (33.3%) improved to normal.⁸

In the study by Baxi K et al¹⁴ there were 8 cases of severe oligohydramnios and 42 cases of moderate oligohydramnios at the time of their first visit. After intravenous amino acids infusion therapy, on repeat USG, 18 (36%) patients with moderate oligohydramnios had improved AFI to normal, whereas 4 patients (50%) with severe oligohydramnios had improved (AFI) to moderate oligohydramnios.

CONCLUSION

Improvement in maternal nutritional status by intravenous amino acid infusion appears to improve the AFI.¹¹ A prospective longitudinal study conducted in 65 pregnant women who attended department of Obs. & Gynae. JNIMS, Imphal, who had reduced amniotic fluid (AFI) proven sonographically, and to see whether any effect of amino acids infusion on AFI or not. It was found that more than two third of the women improved their AFI from their baseline level after the final infusion. There was increased chance of maternal and fetal complications among oligohydramnios and it increased with the severity. However, this study has its own limitation as there are many causative factors of oligohydramnios, so, role of amino acids alone cannot attributed to increase or decrease of AFI. Further, as study was confined to one particular geographical place only and many potential confounding factors could not be evaluated, the finding result cannot be generalized. Further study with a bigger sample size, drawing various confounding factors and with robust studies like RCT will be needed.

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